

Geuvadis - Geneva meeting

Study of alternative splicing

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Analysis

- Contribution of alternative splicing in the transcript abundance variability.
- Splicing QTL discovery.
- Comparison of the splicing patterns between different groups.
→ Which groups to study ?

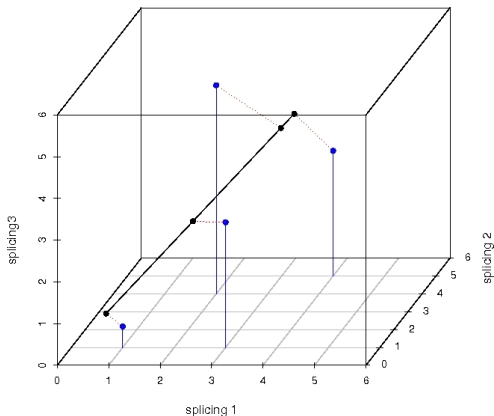
Variability: Gene expression vs Alternative Splicing

Sample A		\Rightarrow	Sample B		\leftarrow Alternative splicing
Isoform 1	10		Isoform 1	90	
Isoform 2	90		Isoform 2	10	
			Sample C		\leftarrow Gene expression
Isoform 1			Isoform 1	90	
Isoform 2			Isoform 2	810	

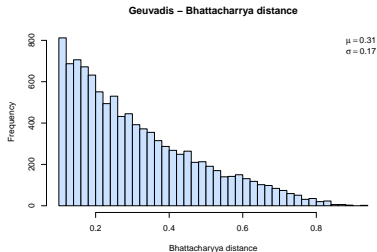
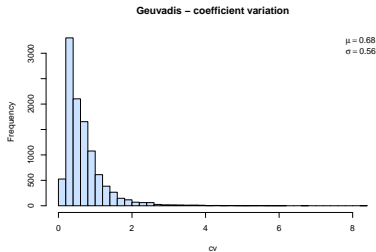
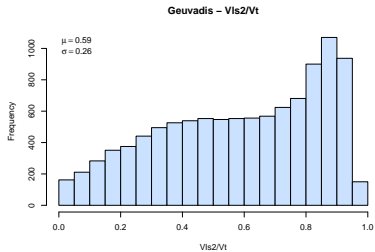
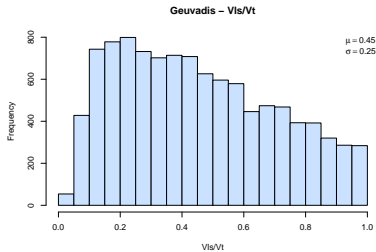
- What is the contribution of gene expression and alternative splicing in the transcript abundance ?

Contribution of alternative splicing in the transcripts' abundance variability

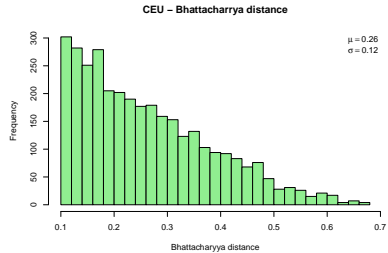
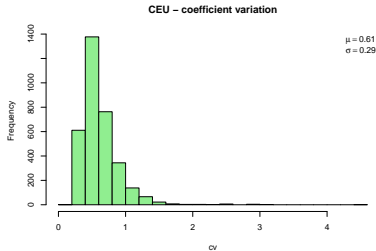
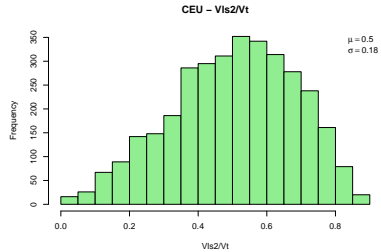
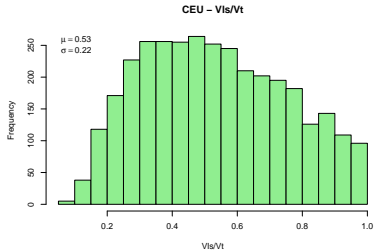
Estimate the ratio $\frac{V_{Is}}{V_t}$ where V_{Is} is the variance when projecting the data to the model of constant splicing ratios and V_t the total variance.



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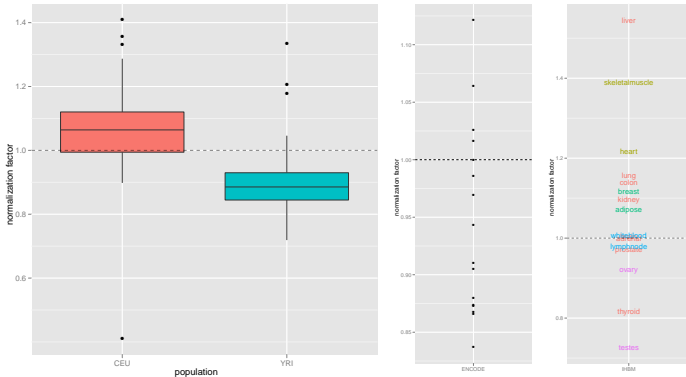


Comparison - CEU



Normalization ?

- Data produced in different laboratories.
- Solution implemented: Trimmed Mean of M-values.
 - Compute a normalization factor for each sample.

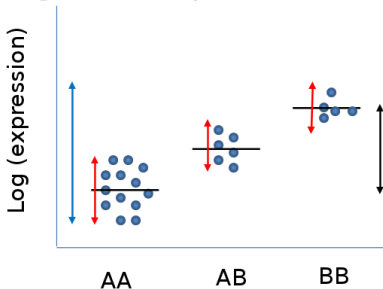


Normalization factor for the populations CEU and YRI together, the ENCODE cell lines and the IHBH tissues. For IHBH tissues, some pairs of tissues are colored with a special color when they should have linked expression patterns because of their biological relation.

Splicing QTL

- Find SNPs changing the splicing behavior of a gene.
- ANOVA-like method.

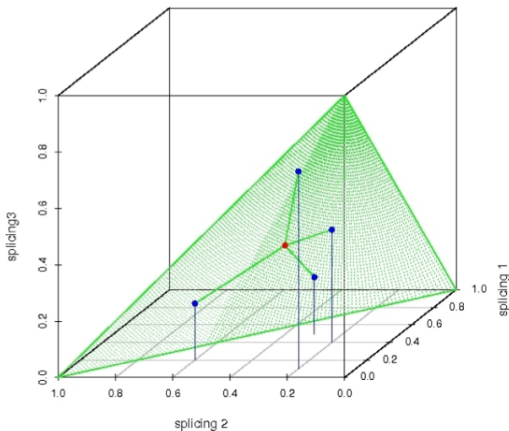
For each gene-SNP pair



Method

For each gene-SNP:

- Computation of a F-ratio like score.
- Permutations and computation of a pvalue.
- False discovery control.



Examples: CEU/YRI

